Claims

1. Method for the detection of a nucleotide sequence in a nucleic acid molecule comprising the following steps:
   (a) hybridization of nucleic acid molecules with a set of different nucleotide base sequences, wherein each probe exhibits a mass different to the mass of all the other probes;
   (b) separation of the non-hybridized probes;
   (c) contact of the hybridized probes with a matrix supporting the desorption of the probes by means of a laser beam;
   (d) analysis of the probes hybridized and surrounded by the matrix on a probe support consisting of electrically conductive material in a mass spectrometer; and
   (e) determination of the nucleic acid molecules exhibiting the sequence, wherein the positions of the probes on the probe support allow for an allocation to the nucleic acid molecule hybridizing therewith.

2. Method according to claim 1, wherein the nucleic acid molecules are transferred to the surface of a carrier before or after step (a).

3. Method according to claim 2, wherein the surface of the carrier is the surface of the probe support consisting of conductive material.

4. Method according to claim 2, wherein before step (c) the carrier with the nucleic acid molecules which are applied to its surface and which carry the hybridized probes is applied to the probe support consisting of conductive material.

5. Method according to claim 2, wherein in step (c) the hybridized probes are separated from the immobilized nucleic acid molecules before, after or through the contact with the matrix.

6. Method according to any one of claims 1 to 5, wherein the probe support has a surface which is metal, coated with glass or chemically modified.

7. Method according to any one of claims 1 to 6, wherein the immobilization of the nucleic acid molecules on the probe support is carried out through a NH_2, an epoxy- or a SH-function by means of coating of the probe support surface with silicate or silane, via protein-substrate-, protein-protein- or a protein-nucleic acid-interaction or via interaction between two hydrophobe components.

8. Method according to claim 7, wherein the protein-substrate-interaction is a biotin-streptavidin-bond or an antibody-antigen-bond.

9. Method according to claim 7, wherein the protein-nucleic acid-interaction is a Gene32-nucleic-acids-linking.

10. Method according to any one of claims 1 to 9, wherein the probes are nucleic acids with a mass tag.

11. Method according to claim 10, wherein the mass tag is also a charge tag.

12. Method according to claim 10, wherein the nucleic acids have an additional charge tag.

13. Method according to any one of claims 1 to 12, wherein the probes are modified nucleic acid molecules.

14. Method according to claim 13, wherein the modified nucleic acid molecules are PNAs, alkylated phosphorothioate nucleic acids or alkylphosphonate nucleic acids.

15. Method according to any one of claim 1 to 14, wherein the probes are produced by combinatorial solid phase synthesis.

16. Method according to claim 15, wherein various base building blocks are marked in such a way that each probe synthesized from them can be differentiated from other probes via its mass in the mass spectrometer.

17. Method according to claim 16, wherein the marking consists of a methyl-, ethyl-, propyl-, a branched or non-branched alkyl-, a halogen-substituted branched or unbranched alkyl-, alkoxyalkyl-, alkylaryl-, arylakyl-, alkoxyaryl- or aryloxyalkyl-group, or one of its deuterated or otherwise isotopic variants.

18. Method according to any one of claims 14 to 17, wherein the probes have at least one modification in a defined position away from randomized nucleotides which allows for cleavage of the probe.

19. Method according to claim 18, wherein the modification is the introduction of a phosphorothioate group and/or an RNA base and/or a phosphotriester bond in the probe.

20. Method according to any one of claims 1 to 19, wherein the matrix is a solution of α-cyano-4-hydroxy cinnamic acid in acetone at a ratio of 1:9 to 9:1, preferably at a ratio of 1:1, or a mixture of α-cyano-4-hydroxy cinnamic acid methyl ester and α-cyano-4-methoxy cinnamic acid or sinapic acid or its methyl derivative at a ratio of 1:9 to 9:1, preferably at a ratio of 1:1.

21. Method according to any one of claim 1 to 19, wherein the matrix is a solution of α-cyano-4-hydroxy cinnamic acid in acetone at a ratio of 1:9 to 9:1, preferably at a ratio of 1:1, or a mixture of α-cyano-4-hydroxy cinnamic acid methyl ester and α-cyano-4-methoxy cinnamic acid or sinapic acid or its methyl derivative at a ratio of 1:9 to 9:1, preferably at a ratio of 1:1, which is applied as solution in acetone, isopropanol, acetonitril, ethanol, methanol or water or in a mixture of two or more of those solvents to the MALDI probe support.

22. Method according to any one of claims 1 to 21, wherein the probes are produced as partial libraries having different mass and/or charge tags.

23. Kit containing
    (a) a set of probes as defined in any one of claims 11 to 18 and/or
    (b) a probe support which has been pre-treated and, thus, allows for the linking of an array of target DNAs and/or contains already bound target DNAs.